

Peer Review File

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Reviewer A

Comment 1: Well-written, thoughtful analysis addressing an important and understudied topic. The methodology and analyses are appropriate and the conclusions well-founded. The authors identify the main limitations of the study (retrospective analyses, small and homogenous sample).

Reply 1: Thank you for the thoughtful feedback on our manuscript.

Changes in the text: N/A

Reviewer B

Comment 1: In the introduction, Please mention any referral criteria / collaborations with PC team

Reply 1: Referral to specialty palliative care was at the discretion of the patients' treating physicians.

Changes in the text: We have added clarification of referral criteria to the Methods section (page 4, lines 16-18).

Comment 2: Page 4 line 9, any guideline, or evidence to support use of earlier PC in quartiles 1-3 (Previous studies eg by David Hui regards earlier PC > 1 or 3 months before death)

Reply 2: Thank you for the suggestion. We have added previous studies on the evidence supporting using of earlier palliative care.

Changes in the text: We have added a sentence describing the rationale for time-based criteria for earlier integration of specialty palliative care and added 3 references (page 5, lines 8-9).

Comment 3: Page 6, line 3, please clarify the types & frequency of specialty PC (eg clinic , home visit). If not, then may mention as a limitation

Reply 3: In the results section, we have added the location of where the first occurrence of specialty palliative care occurred (48.1% in the inpatient setting and 51.9% in the outpatient setting). No palliative home visits occurred in this study population.

Changes in the text: Please see page 7 lines 12-14 for the additions.

Comment 4: Page 6, line 14 , specialized PC teams (teams duplicate here) and oncology teams

Reply 4: We have removed the first mention of “teams” to improve concision.

Changes in the text: The change has been made on page 9, line 10.

Comment 5: In table 2, Please provide median duration for quartile 1-4

Reply 5: We have added the median duration for each quartile as a footnote to Table 2.

Changes in the text: Please see Table 2 for the change.

Comment 6: Fig 3, please provide more details for the non-pain symptoms eg fatigue, insomnia

Reply 6: We have added details for the non-pain physical symptoms to the legend for Figure 3.

Changes in the text: Please see the legend for Figure 3.

Comment 7: Discussion. Local disease although incurable may receive RT but excluded in your study. Please also mention as a limitation.

Reply 7: In the Discussion section, we have added the lack of inclusion of incurable local disease as a limitation. In the Methods section, we have changed the description of “advanced” to “metastatic” to clarify that our study cohort includes patients with metastatic disease. We have also added “among patients with metastatic cancer” to the title to clarify the population.

Changes in the text: Please see title page, page 4, line 9, and page 12, lines 24-25 through page 13, line 1.

Reviewer C

Comment 1: This is an interesting article. However, I do have some comments/questions.

First of all, I miss the benefit of early PC for the patients in this study. This may be due to the retrospective nature of this study, but I feel that this should be specifically addressed; Maybe by putting in a comment that palliative follow-up should include general QoL assessment in the discussion etc. Data on the benefit of early PC is reported in this article from other studies, but I see no effect of early PC on this patient population.

Reply 1: The focus of the study is determining how specialty palliative care and palliative radiotherapy visits and symptoms are distributed over time, along with identifying predictors of earlier specialty palliative care utilization. As the aim of the

study was not to determine the benefit of early palliative care and there are many randomized controlled trials that show a benefit of early palliative care, we did not conduct any analyses to explore this.

Changes in the text: N/A

Comment 2: Introduction, pg 3, line 8: there is a comment on the lack of PC in radiation-oncologists (ROs). As ROs are seldom the ones coordinating the multidisciplinary care for palliative patients I wonder if they should be the ones referring patients to PC, as that could cause conflict with the medical oncologists who often regard the patients as 'theirs'. I would move this line to the comments completely and add more information and data about the difficult role of ROs in multidisciplinary palliative care.

Reply 2: We have removed the sentence in the Introduction on lack of dedicated palliative care training among radiation oncology training programs as suggested. In the Discussion, we present the current uncommon occurrence of palliative care training among radiation oncologists as an opportunity for improving multidisciplinary palliative care through educational initiatives. Radiation oncologists often see patients more evenly across the survival continuum and the comparatively earlier occurrence of palliative radiotherapy consultations presents a unique opportunity for radiation oncologists to not only assess patients' symptoms for the purpose of determining utility of palliative radiotherapy, but also to co-manage symptoms and refer patients (either directly or indirectly via collaboration with a patient's medical oncologist) to palliative care. Integrating the perspectives of radiation oncologists as they're seeing patients may provide an opportunity for more streamlined and timelier referral of patients to specialty palliative care.

Changes in the text: Please see the removal of the sentence on page 3 and the additions on page 10, lines 9-12 and lines 17-20.

Comment 3: Methods: p3, line 33: I assume that haematological patients are excluded due to their disease trajectory which is less predictable disease trajectory than those presenting with solid tumours? Please explain.

Reply 3: Patients with hematologic malignancies were excluded as they are not commonly treated with palliative radiotherapy. Furthermore, as this reviewer notes, those with hematologic malignancies who receive palliative radiotherapy are often patients with a disease trajectory quite distinct from that of metastatic solid malignancies, e.g., cutaneous T cell lymphomas and follicular lymphomas.

Changes in the text: Please see page 4, lines 10-12.

Comment 4: Results: line 28 patient characteristics: this is a fairly young patient

population, which can also be a reason for late PC referral. Please add this to your discussion. Do you have a reason for this relatively young population?

Reply 4: Thanks for the suggestion. We have added the relatively young patient age as a potential reason for late palliative care referral to the Discussion in the limitations section. Our institution is a tertiary academic cancer center and many patients are referred to our institution. We often see patients with very advanced disease.

Changes in the text: Please see page 13, lines 5-7.

Comment 5: I have a question on the topic of hospice referral outcome (p6): is there a possibility to be referred home with palliative home care? In literature, there is data that most patients prefer to die at home, so hospice referral of 73% for me is very high.

Reply 5: Hospice referral of 73% represents referral to any kind of hospice, including home with hospice services, inpatient hospice, or a non-hospital affiliated hospice facility.

Changes in the text: Please see page 8, lines 20-21 for the clarification of what hospice services entailed in our study population.

Comment 6: Discussion, p7, line 30: comment on hope. Please add a reference with data that early PC has proven not to reduce hope. There are several interesting articles that have proven the benefit of early PC on mental wellbeing/hope and this cannot be stressed enough.

Reply 6: We have added a sentence and references on the benefit of early palliative care on well-being and sustaining hope.

Changes in the text: Please see page 12, lines 2-4.

Comment 7: Discussion, p7, line 37: see my earlier comment on hospice referral: I think 73,3% of hospice referral is very high. This could be a cultural difference, but please explain why this is seen as 'only 73.3%' as written in the text. The comment on 10% of patients receiving treatment in their last weeks of life is more interesting and relevant in my eyes, so I would start with this.

Reply 7: We have rewritten the sentence to start with the comment on 10% of patients receiving anti-cancer treatment within 30 days preceding death and removed the mention of "only."

Changes in the text: Please see page 12, lines 7-8 and page 13 line 15 (removal of word "only").

Reviewer D

Comment 1: This is a very interesting, well written and relevant paper which reflects the current challenges faced in palliative care and palliative radiotherapy. The STROBE statement criteria have been met throughout.

Reply 1: Thank you for your thoughtful feedback.

Changes in the text: N/A

Comment 2:

I found the methods section of the abstract somewhat unclear. This reads as quartile 4 represents metastatic diagnosis to death. The quartiles are more clearly described within the methods section of the paper- paragraph study parameters and end points.

Reply 2: We have added a phrase to the methods section of the abstract to clarify what the quartiles represent.

Changes in the text: Please see page 2, line 8.

Comment 3: The paper highlights the benefits of early palliative care intervention and the need for a joined up care approach between palliative medicine and radiotherapy/ chemotherapy. There is a focus within the methods, results and discussion sections on chemotherapy and patients receiving early palliative care. Perhaps the title of the paper should also include anti-cancer treatment.

Reply 3: We have changed the title to include “anti-cancer treatment near end of life.”

Changes in the text: Please see the change to the title on page 1.

Comment 4: Referral for early palliative care at the time of radiotherapy is an intervention recommended within the conclusion. However there is no mention/ recommendation here relating to chemotherapy and the need for early palliative care intervention, as suggested in the methods and discussion sections.

Reply 4: We discussed our finding that patients who received more prior lines of chemotherapy were more likely to have later specialty palliative care in the Discussion section on page 11. We speculate that misconceptions on the purpose of palliative care and a desire to hold out for more aggressive therapy may have led to a delay in referral to specialty PC for patients who received multiple prior palliative chemotherapy regimens. Our recommendation related to the multiple regimens of palliative chemotherapy are for early PC to facilitate goals of care conversations that may reduce aggressiveness in end-of-life treatment. We have added this clarification to the Conclusions.

Changes in the text: We have added clarification that earlier goals and prognosis discussions may decrease “aggressiveness in end-of-life anti-cancer treatment” (see page 12, line 5 and page 13, line 20).

Comment 5: The discussion suggests initiatives to improve clinician's communication skills regarding transitions in goals of care from anti-cancer treatment to hospice. Perhaps it is worth adding that such initiatives to improve communication could also result in earlier palliative care intervention for both radiotherapy and chemotherapy patients.

Reply 5: We have added that communication initiatives may result in earlier specialty PC intervention for patients with metastatic cancer.

Changes in the text: Please see page 12, lines 18-19.

Reviewer E

Comment 1: This is a very informative manuscript characterizing the care paths of cancer patients as they approach the end of their lives. It gives a portrayal of the utilization of palliative care and palliative radiation during their cancer trajectories.

Reply 1: Thank you for your feedback.

Changes in the text: N/A

Comment 2: The only question that I have pertains to whether the authors evaluated whether there was a difference in the prescription of palliative radiation based on whether patients were seen earlier vs. later by Specialty PC. Did earlier specialty PC integration into patient care reduce palliative RT being given within 30 days of life? Were there more single fraction palliative RT vs. multi-fraction RT being given to patients who were seen by Specialty PC earlier? I think Figure 2 gives a hint, but it would be nice to include a description of this data within the text.

Reply 2: We have added Fisher's exact analyses examining the association between earlier specialty PC and incidence of anti-cancer therapy and palliative RT within 30 days of life. We have added a comparison of use of single vs multi-fraction RT across patients who received earlier, later, and no specialty palliative care. Of note, all patients in this cohort received palliative radiotherapy whereas only a portion of patients received specialty palliative care. As such, this study is not adequately powered to investigate the impact of earlier specialty palliative care on changes in palliative radiotherapy fractionation.

Changes in the text: Please see page 5, lines 20-22; page 7, lines 2-8; and page 9 lines 5-7.

Comment 3: I also feel that Figure 2 is slightly misleading by using raw counts at the Y axis given the difference in denominators for each category (Early Specialty PC,

Late Specialty PC and No Specialty PC). Can this figure be reformatted in % events based on the number of patients seen per category? Maybe include this as Figure 2b?

Reply 3: We have created Figure 2b that visualizes the events in percentages across each quartile.

Changes in the text: Please see Figure 2b and page 7 lines 2-8 in the manuscript.